IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Eric BORNSTEIN
Title:	NEAR INFRARED MICROBIAL ELIMINATION LASER SYSTEM
Appl. No.:	10/776,106
Filing Date:	2/11/2004
Examiner:	David M. Shay
Art Unit:	3735
Confirmation Number:	2676

DECLARATION OF DR. ERIC BORNSTEIN UNDER 37 CFR §1.132

Under 37 CFR §1.132 and regarding the rejection of claims 35, 47 and 48 under 35 U.S.C. §102(e) and §103(a) in view of various cited references, being the inventor of the subject matter that is described and claimed in the above captioned patent application, I hereby declare as follows:

1. I am the Chief Scientific Officer and founder of Nomir Medical Technologies, Inc., the assignee of the above captioned application. I have held this position from the inception of the company in 2003 to the present.

2. From the period of 1993-2006, I built and operated a successful private dentistry practice in the Commonwealth of Massachusetts. I am in good standing with the Board of Dentistry and my professional license is current. A brief synopsis of my prior educational and professional background is hereby presented.

a. UNIVERSITY OF VERMONT. 1985-1988. Bachelor of Science Biochemistry.

b. TUFTS UNIVERSITY SCHOOL OF DENTAL MEDICINE. 1988-1992. Doctor of Dental Medicine.

c. MAIMONIDES MEDICAL CENTER. 1992-1993. General Practice Residency.

3. As a practicing dentist, I have extensive experience with the diagnosis and treatment of disorders characterized by infectious microorganisms, as well as with infection control and sterile technique. Microbial infection, and the effects of infection in the oral cavity and systemically, are at the essence of dental practice. In my dental practice, for various types of dental treatments e.g., to control infection, remove biofilms or to ablate infected or necrotic tissues, I have used medical laser-based systems.

4. I have also consulted for medical device companies in the areas of photobiology and laser based medical/dental procedures. My roles have involved providing technical assistance and training, supporting development of new technologies and treatment protocols for dental lasers, as well as providing management and sales advice. I have successfully created and implemented safe and efficacious laser dosimetry parameters for 6 IRB approved human laser clinical studies treating Onychomycosis, MRSA infections in the nose and periodontal disease for Nomir Medical Technologies.

5. I consider myself qualified to present the following statements and conclusions as I believe I exemplify the hypothetical legal person that is "one of ordinary skill in the art"; specifically in connection with medical laser systems; microbiology, infection control and treatment, and; various medical and dental procedures. In support of this position, I have presented at certain conferences indicated or published the following selected papers, these examples deemed particularly relevant to my testimony herein.

a. Bornstein, E., Crown lengthening using the OpusDuo combination Er:YAG and CO2 laser. Dental Products Report, January, 2003

b. Bornstein E, Combining multiple technologies to perform minimally invasive laser-assisted dental implant surgery. Dent Today. 2003 Jun;22(6):52-5..

c. Bornstein, E., A laser technique for frenum removal. Dental Equipment & Materials September, 2003

d. Bornstein E, Lomke MA, The safety and effectiveness of dental Er:YAG lasers. A literature review with specific reference to bone. Dent Today. 2003 Oct;22(10):129-33. (Peer- reviewed)

e. Bornstein E, Why Wavelength and Delivery Systems are the Most Important Factors in Using a Dental Hard-Tissue Laser: A Literature Review, Compendium. 2003 Nov; Vol 24, No 11, pp837-847. (Peer- reviewed)

f. Bornstein E, Near-infrared dental diode lasers. Scientific and photobiologic principles and applications.Dent Today. 2004 Mar;23(3):102-8. (Peer- reviewed)

g. Bornstein E, Proper Use of Er:YAG Lasers and Contact Sapphire Tips When Cutting Teeth and Bone: Scientific Principles and Clinical Applications, Dent Today. 2004; Aug. (Peer- reviewed)

h. Bornstein E.. Method and Dosimetry for Thermolysis and Removal of Biofilm in the Periodontal Pocket with Near-infrared Diode Lasers, Dent Today.2005 April 24 (4): 60-70. (Peer-reviewed)

i. Bornstein ES, Robbins AH, Michelon M: Photo-Inactivation of Fungal Pathogens That Cause Onychomycosis In Vitro And In Vivo With The Noveon Dual Wavelength Laser System.Peer-reviewed abstract presented at New Cardiovascular Horizons, New Orleans, LA, 2008.

j. Bornstein ES, Krespi YP, Robbins AH, et al: Antimicrobial Resistance Reversal At Physiologic Temperatures In MRSA In The Nares With An 870 Nm And 930 Nm Dual Wavelength Noveon Laser. Peer-reviewed abstract presented at TERMIS NA, San Diego, CA, 2008.

k. Bornstein ES and Michelon M: Examining the Antibacteroial Action Spectrum in vitro of the Noveon ® Dual Wavelength Laser System through Photo-inactivation of E. coli at Physiologic Temperatures. Peer-reviewed abstract presented at ASLMS, National Harbor, Maryland, 2009.

l. Bornstein ES: An overview of a Unique Dual Laser System for the Treatment of Infections. Peer-reviewed abstract and presentation given to the Council for Nail Disorders, AAD Meeting, San Francisco, CA March 5, 2009

m. Bornstein ES, A Review of Current Research in Light-Based Technologies for Treatment of Podiatric Infectious Disease States, J Am Podiatr Med Assoc, July/August 2009

6. I have read and understand the rejection of claims 2, 8, 34, and 37 under 35 U.S.C. §102(e) as being anticipated by Goodman. Goodman is cited as anticipating the first wavelength of "about 870 nm". However, upon review that specific wavelength does not appear to actually disclosed by Goodman. The closest frequency disclosed is seen at Paragraph [0247] describing that "at 880 nm… there is a much smaller difference in the between the absorbtion coefficients between the two wavelengths". Likewise Paragraph [0248] describes the isobestic point for hemoglobin at "approximately 880 nm". Goodman doesn't overlap the ranges I claim, which are 865-875 nm and 925-935 nm.

7. I have read and understand the rejection of claims 2, 8, 34, 37, 45 and 46 under 35 U.S.C. §102(e) as being anticipated by Tromberg et al. The Office asserts that the wavelength of Tromberg et al is "about 870 nm" and "about 930 nm". Tromberg et al provides an

apparatus for performing frequency domain photon migration measurements on turbid media (breast tissue). Frequencies described are general ranges from 600 nm to 1200 nm; and specific frequencies of 672, 800, 806, 852, 896, 913 and 978 nm (see paragraph 0021). The specific frequencies cited by Tromberg et al do not overlap the ranges I claim, which are 865-875 nm and 925-935 nm; although the broad disclosure covers the range from visible red, through mid-IR, it does not recognize with specificity, the antimicrobial effects of the two claimed narrow bands in the near IR spectra. The Tromberg et al reference lacks any disclosure about antimicrobial effects, so in addition to lacking any specificity as to my claimed ranges, the reference doesn't appreciate the specific antimicrobial properties of these ranges.

8. I have read and understand the rejection of claims 2, 8, 34, 37, 45 and 46 under 35 U.S.C. §102(e) as being anticipated by Merilainen. The Office asserts that the wavelength of Merilainen is "about 870 nm" and "about 930 nm". The Merilainen reference provides a similar case as Tromberg et al. The Merilainen paper describes general ranges of frequencies from 600 nm to 1000 nm; and specific frequencies of 775, 810, 850 and 913 nm (see Column 6, lines 25-30). None of the specific frequencies recited are in my claimed ranges, but the broader disclosure encompasses the claimed ranges. Like Tromberg et al, the Merilainen reference lacks any disclosure about antimicrobial effects, so in addition to lacking any specificity as to my claimed ranges, the reference doesn't appreciate the specific antimicrobial properties of these ranges.

9. Near infrared wavelengths are employed in the prior art devices because of their tissue penetration properties; but none of the cited references recognize the specific wavelengths 865-875 nm and 925-935 nm, or that these ranges are critical because these are the frequencies that provide for the cytotoxic effects of my invention. The cited references don't appreciate the effect of power output in these critical frequency ranges, and can't render my invention obvious without recognizing this important feature.

10. Importantly, none of the cited references (Goodman, Tromberg et al. and Merilainen) offered as anticipating the claimed invention, teach that *the power delivered by the first and second wavelengths is the majority of the total power of near infrared radiation output by the device.*

11. I have read and understand the rejection of claim 35 under 35 U.S.C. §103(a) as being unpatentable over Goodman in combination with Grable. The Office asserts that "Goodman teaches a devices as claimed, but does not disclose a particular power. Grable teaches that powers in applicant's disclosed range are appropriate for diagnosing tissue. It would have been obvious… to employ the laser power of Grable in the device of Goodman, since this would produce the power necessary for determining the desired tissue parameters, thus producing a device such as claimed"

12. I have read and understand the rejection of claims 35, 47 and 48 under 35 U.S.C. §103(a) as being unpatentable over Tromberg et al in combination with Grable. The Office asserts that Tromberg et al "teach a device as claimed, but do not disclose a particular power. Grable teaches that powers in applicant's disclosed range are appropriate for diagnosing tissue. It would have been obvious… to employ the laser power of Grable in the device of Tromberg et al, since this would produce the power necessary for determining the desired tissue parameters, thus producing a device such as claimed"

13. I have read and understand the rejection of claims 35, 47 and 48 under 35 U.S.C. §103(a) as being unpatentable over Merlainen in combination with Grable. The Office asserts that Merlainen "teach a device as claimed, but do not disclose a particular power. Grable teaches that powers in applicant's disclosed range are appropriate for diagnosing tissue. It would have been obvious… to employ the laser power of Grable in the device of Merlainen, since this would produce the power necessary for determining the desired tissue parameters, thus producing a device such as claimed"

14. Regarding power output, the power outputs given in my invention are not directly equivalent to those disclosed by Grable. To compare these values, one needs to adjust for the pulse lengths. Doing so, by way of comparison my invention provides for an approximate 8 Log reduction in unit energy per/pulse as compared to that of Grable.

15. It is my opinion, that a person skilled in the medical laser field would not combine the cited references the way the Office describes, when approaching the problem of developing a laser based phototherapeutic antimicrobial device from the devices of Goodman, Tromberg et al, and Merilainen, based on the power settings disclosed in Grable. The power outputs described by Grable, when applied to the devices of Goodman, Tromberg et al, and Merilainen, would cause substantial tissue damage to any subject exposed to the laser beam. Grable itself supports this conclusion, and specifically discloses that their resultant laser beam needs to be optically dispersed or swept in order to disperse the beam energy.

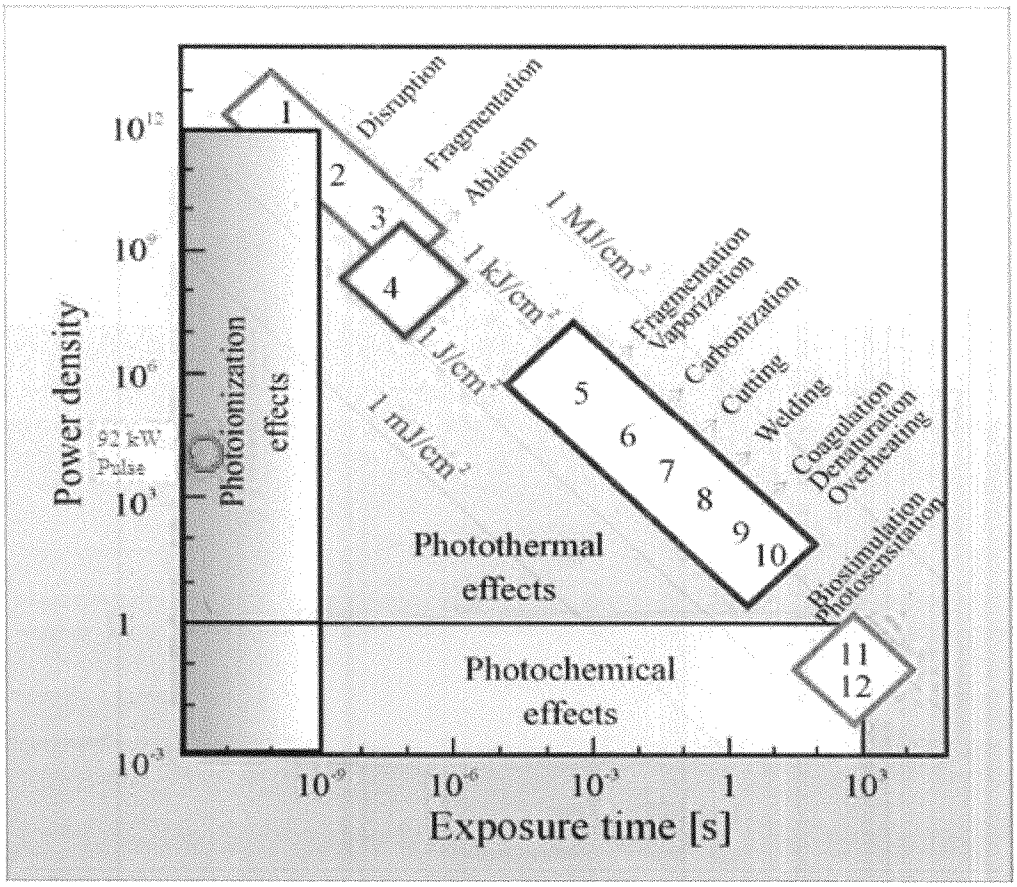
16. It would not be appropriate to use the power levels of Grable in the device of Goodman. Calculating the peak power output for any theoretical pulsed laser with a square pulse shape, we see:

a. Average Output Power (W) / Rep Rate (Hz) / Pulse Duration (microseconds) = Peak Power/Pulse (W).

b. Substituting the appropriate values for the Grable laser, the calculation is thus: (0.75 W) / (76,500,000 Hz) / (0.000000000000106 s) = 92.5 kilowatts/pulse.

c. Note that Paragraph 0056 of the Grable specification states that the Peak Power/Pulse is 67 kw/pulse, consistent with the above approximation. This difference may due to the particular shape and width of the Grable pulse.

17. A peak power of 67 kW/pulse is a tremendous amount of energy if it is applied to a single point. Femtosecond lasers with average power outputs of 0.75W are ablative in nature with very high peak power outputs. This is the principle behind photo-ionization effects with lasers. This can be illustrated with the following figure, illustrating the effects of Power Density over Time.



18. Regarding the specific rejection of claim 35 under 35 U.S.C. §103(a) as being unpatentable over Goodman in combination with Grable, I disagree that the combination renders the claims obvious. The power outputs of Grable, when used in the device of Goodman, would produce a high power/small spot device that would severely damage any tissues the emitted light contacts. The only reason the Grable power levels are safe for use in the laser-based diagnostic device described, is that Grable uses optics to spread

the fast-pulsed beam out over multiple angles to form a fan shaped beam. In alternate embodiments, where Grable applies the laser by sweeping the laser beam itself across the breast (instead of using a lens/mirror system to diverge the laser beam into a fan), Grable notes that one must decrease the power applied to the diagnostic site to levels lower than those listed for the primary embodiment. As one of skill in the art, it is my opinion that the one similarly skilled would not combine the power levels of Grable with the device of Goodman.

19. Regarding the rejection of claims 35, 47 and 48 under 35 U.S.C. §103(a) as being unpatentable over Tromberg et al in combination with Grable, I disagree that the combination renders the claims obvious. This rejection is similar to that discussed in Paragraph 18 above, in that Grable is cited as teaching the powers in applicant's disclosed range are appropriate for diagnosing tissue. I restate the arguments presented above in terms of the power output of the Grable device. Tromberg et al describe scanning systems for imaging tissues of a patient, and gives specific examples of using lasers tuned to near-IR frequencies, to analyze breast tissues for abnormalities. The Tromber device is applies laser light to a "delivery point" on a turbid media, e.g. breast tissue of a human patient. Applying the power settings of Grable to the Tromberg et al device would produce an apparatus that would injure the patient. The power output of Grable in the Tromberg et al device would cause tissue damage/ablation to the imaged breast tissue. Since the proposed combination would not disperse the resultant beam to diffuse the power (as the primary embodiment of Grable does) this particular combination is prone to cause injury. As one of skill in the art, it is my opinion that the one similarly skilled would not combine the power levels of Grable with the device of Tromberg et al.

20. Regarding the rejection of claims 35, 47 and 48 under 35 U.S.C. §103(a) as being unpatentable over Merlainen in combination with Grable, I disagree that the combination renders the claims obvious. This rejection is essentially the same as that discussed in the Paragraphs 18 and 19 above, and those arguments are restated in this context. Applying the power settings of Grable to the Merlainen device would produce an apparatus that would injure the patient. Merilainen describes constant irradiation of brain tissue to measure anaesthetic responses. Clearly, the power outputs of Grable are unsuitable in the Merilainen device—the patient's brain and skull would be perforated by the laser. As one of skill in the art, it is my opinion that the one similarly skilled would not combine the power levels of Grable with the device of Merlainen.

21. A person of skill in the art would recognize that the diagnostic devices described by Grable, Goodman, Tromberg et al, and Merilainen are designed for long beam exposure times, in that the devices are meant to be employed as monitoring or scanning devices. As such a skilled artisan would recognize the undesirability of using high levels of energy/pulse, in devices where the subject will have a long exposure time to the laser beam. The Examiner is again referred to the illustration in Paragraph 17.

22. I submit that the Neumann paper, which has been extensively discussed by the Examiner and the Applicant during prosecution of this case, is considered by those of skill in the laser arts as a landmark study in the mechanical properties of lasers, and is demonstrative of the state of the art in near IR laser technology following its publication. Neumann teaches the specific wavelengths 865-875 nm and 925-935 nm have cytotoxic effects to eukaryotic and prokaryotic cells. This paper would have been available to Grable, Goodman, Tromberg et al, and Merilainen, as they developed their products having infrared lasers, and Neumann would have contraindicated the use of these specific cytotoxic wavelengths. I conclude this may be why these references do not employ such wavelengths. Particularly, and as discussed in Paragraph 21, a skilled artisan and Grable, Goodman, Tromberg et al, and Merilainen themselves would have understood in view of Neumann not to use cytotoxic frequencies in long exposure or high power output applications.

23. The §103 rejections above are predicated on the common theme of a laser device using one or more IR frequencies. I note the use of specific frequencies, but Goodman, Tromberg et al, and Merilainen do not teach the properties of, or the specific frequencies ranges I claim, nor does any reference teach that *the power delivered by the first and second wavelengths is the majority of the total power of near infrared radiation output by the device*. Grable does not teach or recognize this property or specific frequencies either.

24. None of the cited references, Grable, Goodman, Tromberg et al, or Merlainen disclose antimicrobial phototheraphy systems and are instead directed to diagnostic sensing and imaging technologies, not for tissue sparing infection control procedures. The devices disclosed therein are inoperative for this purpose, in any combination.

25. The problem of microbial infection is persistent, and offers constant challenges to hospitals, medical offices, and health care personnel. Patient effects from microbial infections can range from chronic infection to lethal septicemia. Massive amounts of money and commitments to research antimicrobial drugs have provided healthcare personnel with chemotherapeutic methods for infection treatment of fungal and bacterial infections, but resistance evolves with the therapeutic use of such drugs. Accordingly, there is a persistent and long-felt need to develop new antimicrobial treatments, particularly in view of evolving antimicrobial resistance.

26. My invention provides for antimicrobial treatments consisting of photodamaging dosages of specific cytotoxic frequencies of near infrared optical radiation. The photodamage to the microbe affects cellular metabolism in a manner very different from the mechanism of antibiotics. As such, my invention addresses this long-felt need to develop new antimicrobial treatments directed toward sensitive microbial cellular targets, which is recognized and persists.

27. My invention addresses a problem of toxicity that has not been solved by others in the field of antimicrobial therapeutic drugs, in that my invention affects both eukaryotic and prokaryotic pathogenic cells, without causing systemic toxic effects in the subject. For example, oral antifungal agents like terbinafine can cause liver and heart damage, and broad spectrum antibacterial agents like ciprofloxacin can damage kidneys. The present invention is applied locally not systemically, and so it avoids systemic toxicity.

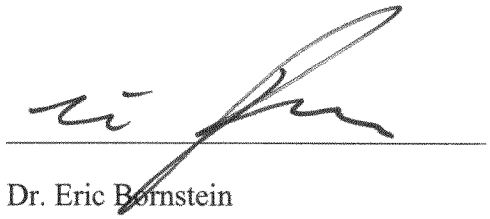
28. My invention also addresses a problem of consequential subject tissue damage at the treatment site that has not been solved by others in the field of medical lasers. To my knowledge, other than high output power laser systems that are used to ablate or thermolyse infected tissues, or damage tissues as an undesired side-effect to direct thermal damage of microbes, there are currently no laser based systems for treating infection other than the instant invention, that can photodamage microbes without causing pain, thermolysis or tissue damage to the treated subject.

29. The instant claims describe the laser apparatus used in the NOVEON^{TM} brand phototherapy system developed by Nomir Medical Technologies, Inc. This product satisfies the long-felt need for an optical antimicrobial system, and it provides patients with a treatment option that eliminates the systemic toxicity problems inherent to chemotherapy, and avoids the detrimental effects of heat deposition and tissue damage of existing therapeutic medical laser systems. Clinical trials of the device and peer review of the data confirm its efficacy, and the findings have received significant interest at professional conferences such as those listed in Paragraph 5, from researchers as well as medical and dental practitioners.

30. The NOVEON^{TM} brand phototherapy system is under review by the FDA for 510(k) medical device registration, and Nomir Medical Technologies, Inc. is currently restricted from selling the device for antimicrobial use. However, as permitted by the FDA, physicians have requested the company reserve devices for their purchase pending FDA approval of the device. Thus, in view of such government restrictions on sales, the apparatus claimed has nevertheless achieved commercial success, as evidenced by physician reservations of Nomir's NOVEON^{TM} brand phototherapy system.

31. I declare further that all statements made in this Declaration of my own knowledge are true, that all statements made on information and belief are believed to be true, and further, that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of any patent that may issue from the present application.

Signed this 20th day of July, 2009, by



Dr. Eric Bornstein